

STATEMENT OF OBJECTIVES

A SYSTEMS BIOLOGY APPROACH TO INFECTIOUS DISEASES RESEARCH

RESEARCH and TECHNICAL OBJECTIVES

This section presents the technical objectives that the Government seeks to achieve through this BAA. Proposals should explain how the offeror will contribute to these overall objectives. Contracts awarded as a result of this BAA will include the Statement of Work proposed by the offeror and negotiated and accepted by the Government.

BACKGROUND and INTRODUCTION:

The National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH), Department of Health and Human Services (DHHS) supports research related to the basic understanding, treatment and ultimately prevention of infectious, immune-mediated and allergic diseases that threaten millions of human lives. The NIAID Division of Microbiology and Infectious Diseases (DMID) supports a comprehensive extramural research program focused on the prevention and control of diseases caused by virtually all infectious agents (with the exception of the Human Immunodeficiency Virus). This includes basic research, such as studies of microbial biology and physiology; applied research, including the development of medical diagnostics, therapeutics and vaccines; and clinical trials to evaluate experimental drugs and vaccines.

The NIAID has made a significant investment in genomic-related activities that provide comprehensive genomic, functional genomic, bioinformatics, and proteomic resources to the scientific community for basic and applied research to rapidly address the Institute's mission and the Nation's biodefense needs (<http://www.niaid.nih.gov/dmid/genomes/>). The NIAID-supported genomics programs include:

- *Microbial Genome Sequencing Centers* provide rapid and cost-efficient production of high-quality genome sequences of human pathogens and invertebrate vectors of diseases.
- *Pathogen Functional Genomics Resource Center* provide functional genomic resources, data and reagents, including DNA microarrays, protein expression clones, genotyping for comparative genomics of pathogenic species, and comparative protein profiling.
- *Bioinformatics Resource Centers* provide a robust point of entry for access of genomic and related data in a user-friendly format, and include databases to host microbial genomic data and analysis centers to develop and provide software tools.
- *Proteomics Research Centers* provide the characterization of the proteomes of pathogens and/or host cells; identify proteins associated with the biology of microbes, mechanisms of microbial pathogenesis, and host response to infection; and discover targets for potential candidates for the next generation of vaccines, therapeutics, and diagnostics.

In addition, the NIAID is also planning to establish, in Fiscal Year 2007, *Structural Genomics Centers for Infectious Diseases* to experimentally characterize the three-dimensional atomic structure of proteins of pathogenic organisms and, in Fiscal Year 2008, *Clinical Proteomics Centers for Infectious Diseases and Biodefense* to identify candidate pathogen and host biomarkers important for infectious diseases.

These genomic programs have not only provided the scientific community with valuable resources, but have also enhanced the NIAID's research efforts in a number of areas including pathogen identification, pathogen virulence, and drug and diagnostics development. Projects within these programs have, for the most part, been conducted to investigate with high-throughput technologies the genome or the proteome of a living organism as independent entities, rather than as two highly interrelated and interdependent components. The purpose of this solicitation is to establish large-scale, coordinated Systems Biology Programs that build upon and expand the publicly accessible genomic and genomic-related data, resources and technologies generated through the NIAID-supported genomic programs.

For purposes of this BAA, "Systems Biology" is defined as the study of an organism, viewed as an integrated cellular system consisting of an *interacting network* of genes, proteins, other molecular cellular components and their biochemical/biophysical reactions.

A systems biology approach offers a strategy that utilizes multiple and integrated high-throughput technologies for conducting a variety of "omics" types of investigations, such as functional genomics, proteomics, metabolomics, glycomics or lipidomics, to comprehensively and simultaneously investigate the multitude of biological molecular processes that characterize the functions of microbial organisms. Systems biology requires a shift in thinking to a more global and high-throughput methodology to identify, quantify, analyze, model and predict the overall behavior and dynamics of the network of molecular components of cells.

The Systems Biology Programs shall use a systems biology approach to comprehensively study molecular pathways (e.g., signaling, regulatory, metabolic) or other types of molecular interaction networks of microbial pathogens and their host cells through a combination of computational and experimental high-throughput technologies. Although a systems biology approach could be used to investigate complex biological events such as cell behavior or microbial communities, the focus of this initiative is only on molecular cellular events of the pathogen and the host, such as those involved in the biological, biochemical and biophysical processes of microbial organisms or in pathogenesis and disease progression in humans. The simultaneous utilization of multiple technologies in a coordinated Systems Biology Program and the integration of heterogeneous "omics" data will highlight distinct aspects and provide exhaustive insights into the biological processes being investigated.

The knowledge generated from this initiative, including experimentally and computationally generated data, experimental protocols, reagents, algorithms and analysis software tools, shall be widely disseminated to the scientific community through publicly accessible databases and reagent repositories. The research findings are expected to provide a deeper understanding of the overall complexity of the biological, biochemical and biophysical molecular processes in bacteria, parasites, or viruses as well as how the molecular events within the pathogen may lead to the initiation and progression of infectious diseases. Such information should identify

novel, unique, as well as common molecular signatures that may represent future targets for intervention and could aid in the identification of emerging pathogens and in the development of antimicrobial drugs, immunotherapies, vaccines and diagnostics for prevention and treatment of diseases caused by potential agents of bioterrorism and emerging/reemerging infectious diseases, thus potentially translating basic research findings into clinical applications.

It is anticipated that this BAA will support the establishment of two to three large-scale collaborative Systems Biology Programs, each composed of multidisciplinary teams of investigators with a wide breadth of skills and scientific and technical expertise. All proposed activities must be completed within the maximum five-year contract period of performance.

The NIAID reserves the right to award all or any portion of the proposed Statement of Work based on technical merit, scientific priority, programmatic balance, and the availability of funds.

BROAD AGENCY ANNOUNCEMENT INFORMATION

You are invited to submit a proposal in accordance with the requirements of this BROAD AGENCY ANNOUNCEMENT (BAA) solicitation BAA NIH-NIAID-DMID-08-22 entitled "A Systems Biology Approach to Infectious Diseases Research." The BAA is authorized by Federal Acquisition Regulation (FAR) 6.102 and further described in FAR 35.016 as well as the NIH Manual Issuance 6035, Broad Agency Announcements. A BAA is a general announcement of an agency's research interest. The intent of a BAA is to encourage the submission of creative and innovative approaches to specific research areas identified by the Government.

A proposal submitted in response to this BAA must present a detailed technical and cost proposal designed to meet the Research and Technical Objectives described in this announcement. The proposal must be signed by an official authorized to contractually commit the submitting organization.

The Statement of Work, including the specific work requirements and performance specifications, is developed and defined by the offeror, not the Government.

Proposals are NOT evaluated against a specific Government need, as in the case of a conventional Request for Proposal (RFP), since they are not submitted in accordance with a common Statement of Work issued by the Government. Instead, Research and Technical Objectives are provided in the BAA that describes the research areas in which the Government is interested. Proposals received as a result of the BAA are evaluated by a Scientific Review Group (SRG) in accordance with the Technical Evaluation Criteria specified in the BAA. NIAID reserves the right to convene multiple SRGs to evaluate proposals.

There is no Source Selection Determination utilized under the BAA process. All the competing proposals are ranked on the basis of their respective relevance and scientific merit. The scores assigned by the SRG are considered the final scores. An Order of Merit Ranking is established by the Contracting Officer in lieu of a Competitive Range.

Negotiations are conducted with offerors selected from the Order of Merit Ranking based on their scientific merit and those specific considerations set forth in this solicitation under Section M, Evaluation Factors. During negotiations, there is an opportunity to refine the proposed Statement of Work in consultation with the Project Officer including the incorporation of comments of the SRG, as appropriate. At the conclusion of negotiations with the offerors selected from the Order of Merit Ranking, those offerors are allowed the opportunity to submit a Final Proposal Revision (FPR), to address weaknesses in the proposal and questions identified by the SRG.

The award document will be tailored to the final negotiations with the selected offeror(s) and modified as appropriate for the type of contractor organization, cost and/or fee arrangements, and other elements as negotiated prior to award.

1) SCOPE:

Contracts awarded under this BAA shall establish large scale, coordinated Systems Biology Programs that utilize a combination of computational and experimental methodologies to conduct research Projects to analyze, identify, quantify, model and predict the overall dynamics of the network of cellular molecular components of microbial organisms and their interactions with the host cells. Each research Project of the Systems Biology Program shall concurrently utilize multiple high-throughput “-omics” technologies to generate a diversity of experimental data. These experimental data shall be collected and, if possible, integrated into other publicly accessible “-omics” datasets, such as those retrieved from the genomic resources established by the NIAID-supported genomic research programs, to develop and/or validate computational models of the molecular interaction networks involved in the biological processes under investigation.

The resources generated by the System Biology Program shall be made publicly available and easily accessible to the scientific community through public data, software and reagent repositories and through web portals. The ultimate goal of the Systems Biology Program is to enhance knowledge of the overall complexity of the biological, biochemical and biophysical molecular processes in microbial organisms and host cells which may lead to the initiation and progression of infectious diseases.

2) TECHNICAL REQUIREMENTS:

Contracts awarded in response to this BAA shall meet the following technical requirements:

A. Systems Biology Program for Infectious Diseases Research

Provide facilities, equipment, technologies, methodologies, and scientific and technical expertise to establish a Systems Biology Program for infectious diseases research that utilizes a system biology approach for the conduct of research Projects to analyze, identify, quantify, model and predict the overall dynamics of the network of cellular molecular components of microbial organisms and their interaction with the host cell.

1) Systems Biology Approach

The systems biology approach must include the following key elements:

- a. Comprehensive analyses of the molecular events. A study may focus on the whole or a substantial portion of the transcriptome, proteome or metabolome of a microorganism. For example: a study may involve unbiased global analyses of multiple biological parameters at multiple time points during the course of an infection or under a variety of experimental cellular conditions.
- b. Advanced computational modeling and simulations to create predictive mathematical representations or dynamic models of the biological molecular processes or reaction networks of the pathogens and hosts under investigation.

- c. A repeating cycle of computational modeling, experimental validation and data mining. For example, a procedure that combines both computational and experimental methodologies to (i) *in silico* model, predict or simulate the overall biochemical or biophysical processes of a micro-organism; (ii) experimentally validate those models using high-throughput technologies; (iii) collect and integrate experimental data to inform and help improve the selection of the model's parameters and variables, or the reliability of the simulated data; and (iv), repeat from (i).

2) Targeted Organisms

The microbial pathogens targeted for the systems biology studies are those in the NIAID Category A-C priority lists for biodefense research (http://www3.niaid.nih.gov/biodefense/bandc_priority.htm) and their phylogenetically related species, as well as pathogens causing emerging/re-emerging infectious diseases. Although proposals that are not directed specifically at the targeted pathogens are considered responsive to this BAA, offerors must be aware that only limited funding is available for such types of proposals.

While this BAA will support studies on the interaction of the pathogen's molecular networks with the molecular components of the cells of the human host or of an appropriate model host organism for human infectious diseases, this BAA will not support studies that focus exclusively on the molecular interaction networks of the host cells. Examples of research areas that are not responsive to this BAA include:

- analysis of host response to infection in the absence of bacterial or viral pathogenesis studies;
- analysis of the host control of expression and signaling through innate immune receptors;
- dissection of the molecules and pathways involved in the regulation of the adaptive immune system; and
- studies of host pathways that regulate antibody production to pathogens or vaccines.

3) Systems Biology Program Research Projects

The Contractor shall propose and conduct one or more research Projects that focus on cellular networks whose key molecular components are known (for example through experimental evidence) or are assumed (for example through computational comparative genomics) to be functionally in common within a pathogenic species or across multiple species. The research findings of such Projects should have the potential to be applicable or relevant to a variety of pathogenic organisms and should lead to a better understanding of the biological, biochemical and biophysical processes of microbial organisms or of the initiation and progression of infectious diseases in humans. Each Project must include the key elements of the systems biology approach delineated in 1) above.

Examples of research projects responsive to this BAA include, but are not limited to, the following:

- predict, identify and quantify changes in whole genome-wide or proteome-wide expression of a number of closely related bacterial or viral species following encounter with the host cells and during various stages of host infection;
- predict, identify and quantify the transcriptional and regulatory response of the host's immune response system against a variety of pathogenic strains of a microbial organism compared with mutant strains that lack key virulence factors;
- predict, identify and quantify the key molecular components and the reactions of metabolic pathways that have functional variants in multiple bacterial pathogens and commensals;
- develop models that predict genes' essentiality in multiple phylogenetically related microbial species and validate through knockout experiments;
- develop models that predict metabolic and regulatory networks that will facilitate the identification of genes that may be coding for virulence determinants and contribute towards the progression of disease in different host cells; verify experimentally;
- develop models that investigate the impact of one pathogen (e.g., *Streptococcus pneumoniae*) on the infection outcome of another (e.g., influenza virus); verify experimentally.

4) High-Throughput Technology Cores

Independent of the biological systems to be studied, the Systems Biology Program shall utilize or improve a combination of high-throughput technologies to generate high quality experimental data in support of the systems biology analyses of the pathogen or of its interaction with the host cells.

- a. First-year Requirement: In the first year through the end of the contract period provide the following three high-throughput technology cores to be used concurrently for each Project:
 - i. Informatics core for experimental data integration and analysis, computational modeling and simulation of the biological systems.
 - ii. Functional genomics core, which may use methodologies, such as gene expression multiplex technologies, genotyping microarrays, Chip-on-Chip, genome-wide analysis of essential genes, and RNAi screens, to characterize the transcriptome of the organisms under investigation in different experimental conditions, for example, by monitoring the host/cell transcriptional response to pathogens, or by identifying cellular/genetic control mechanisms.
 - iii. Proteomics core, which may use high-throughput methodologies, such as protein arrays, yeast two-hybridization and mass spectrometry, to characterize the proteome of the organisms under investigation by identifying and quantifying the cellular levels of each protein encoded by the genome.
- b. Second-year Requirement: In the second year through the end of the contract period the Systems Biology Program shall focus not only on the transcriptome and proteome of the living organisms under investigation,

but also on other important and more diverse set of cellular components to investigate the cell molecular networks, by utilizing existing or emerging high-throughput technologies. Within the second year of the contract period, the Contractor shall provide at least one of the following three high-throughput technology cores for each Project:

- i. Metabolomics core, which may use high-throughput technologies, for example, to identify the complete set of metabolites of the pathogen and host cells and to investigate the dynamic response of the biological system to genetic or chemical perturbations.
- ii. Glycomics core, which may use high-throughput technologies, for example, to perform large-scale analysis of the structure and function of the complete set of glycans and glycan-binding proteins expressed by the pathogen and host cells and to investigate the dynamic response to genetic or chemical perturbations.
- iii. Lipidomics core, which may use high-throughput technologies, for example, to identify and measure the set of chemically distinct lipids in the pathogen and host cells, and to determine the molecular mechanisms through which they impact cellular functions.

5) Multidisciplinary Scientific and Technical Research Teams

The Contractor shall provide multidisciplinary research teams of investigators with the breadth of complementary skills and expertise required to implement the negotiated Statement of Work. The multidisciplinary research teams shall combine diverse scientific and technical expertise in biomedical sciences (e.g., microbiology, infectious diseases, immunology), high-throughput technologies (e.g., for proteomics, glycomics), quantitative sciences (e.g., mathematics, physics, computer science), and bioinformatics and information technology. Diverse research teams may be located at one institution or may be formed through subcontracts at different institutions. In either case, the Contractor shall establish a well integrated and collaborative environment, with frequent interactions and communication with members of the research teams.

B. Provision of Contract-Generated Resources to the Scientific Community

The Contractor shall make the data and resources generated by the Systems Biology Program publicly available and easily accessible to the scientific community.

1) Plan for the Public Release of Contract-Generated Resources

The Contractor shall develop and implement a Plan for the Public Release of Contract-Generated Resources that includes the following overall guidelines and information:

- a. The release to the scientific community within four (4) weeks from publication, or within one (1) year of generation, whichever comes first and as agreed upon by the Project Officer, of contract-generated resources, such as experimental and computationally generated research data, metadata, statistical and simulated data, statistical models,

experimental protocols, novel reagents (e.g., expression vectors, expression arrays, libraries, protein clones), database schema and computational algorithms and data analysis tools.

- b. A detailed list of the resources to be generated during the performance of the contract, specifying which resources will be placed in the public domain within four (4) weeks from publication or within one (1) year of generation.
- c. Expected timelines for public release of contract-generated resources.
- d. The public repositories to be used to publicly disseminate contract-generated resources. Include a summary of the discussions and documentation on agreements between the Contractor and the public repositories regarding the transfer and dissemination of data, reagents and software.

Within three (3) months of contract award, the Contractor shall submit to the Project Officer and the Contracting Officer for review and approval, a Plan for the Public Release of Contract-Generated Resources. The plan shall be revised/updated on an annual basis as part of the Annual Progress Report. The Plan and its updates are subject to modifications by the Project Officer and the Contracting Officer prior to their approval.

2) Systems Biology Program Web Portal

The Contractor shall design, implement and maintain a public website that:

- a. describes the Systems Biology Program, its mission, specific research Projects and research teams;
- b. lists relevant publications and useful links, news and events;
- c. provides easy access to contract-generated data, software, models and protocols, using standard formats and exchange protocols, if such standards exist;
- d. provides links to contract-generated data and software submitted for public dissemination to other public repositories, such as the NIAID Bioinformatics Resource Centers (BRCs) (<http://www.niaid.nih.gov/dmid/genomes/brc/default.htm>);
- e. provides links to protocols and reagents submitted to the NIAID Biodefense and Emerging Infections (BEI) Research Resources Repository (www.beiresources.org) or public reagent repositories;
- f. captures web site access metrics, such as the total number of external visits, the pages most frequently viewed, the number of times contract-generated resources are downloaded, as well as more detailed descriptions of web site usage as requested by the Project Officer; and
- g. is Section 508 compliant (<http://www.section508.gov>).

Within two (2) months of contract award, the Contractor shall launch the first release of the publicly accessible web portal. The Project Officer shall be notified and be given preview access to all the releases seven (7) calendar days before the release takes place.

3) Contract-Generated Data and Software

Contract-generated data and software shall be made available through publicly accessible web and database sites, including the Systems Biology Program Web Portal, the BRCs (<http://www.niaid.nih.gov/dmid/genomes/brc/default.htm>), and/or other public repositories, as identified by the Contractor in consultation with the Project Officer.

Contract-generated data and software include, but are not limited to:

- a) all research data (both experimentally and computationally generated);
- b) all the metadata for the research data in a);
- c) database schema and specifications;
- d) experimental protocols and Standard Operating Procedures (SOPs); and
- e) data analysis software, implemented statistical models and algorithms generated under this contract, including their object and source code, complete use documentation and tutorials.

Whenever possible, the Contractor shall provide software certified by the Open Source Initiative (<http://www.opensource.org/licenses/>), to guarantee the right to read, redistribute, modify, and freely use the software.

4) Contract-Generated Reagents

The Contractor shall submit, for dissemination to the scientific community, contract-generated novel reagents (e.g., expression vectors, expression arrays, libraries, protein clones), to existing repositories, such as the BEI, or other repositories as identified by the Contractor in consultation with the Project Officer.

C. Information Technology and Data Management

1) Plan for Developing and Maintaining the Information Technology and Data Management Systems

Within two (2) months from contract award, submit to the Project Officer and Contracting Officer for review and approval, a Plan for Developing and Maintaining the Information Technology and Data Management Systems of the Systems Biology Program. An update to the Plan shall be submitted within one (1) month after the end of the third year of the contract period of performance. The Plan and its update are subject to modifications by the Project Officer and Contracting Officer prior to approval. The Plan shall include, at a minimum, a description of the computational and network infrastructure provided by the Contractor; an overview of the security and privacy requirements; logical access control to networks and information systems, remote access, monitoring, etc.; the methods used for protection against data loss; malicious code protection (e.g., antivirus, filtering of e-mail attachments, etc.); security awareness training requirements for the Contractor and subcontractors staff; and physical security, such as access control (e.g., locks, guards), power conditioning, air conditioning, fire protection.

Provide similar information for any subcontractor developing or accessing the Systems Biology Program's information technology infrastructure and network.

2) Data Management System

Implement and operate a data management system for the secure storage, quality control, integration and overall management of all data and experimental results generated by the Systems Biology Program, including the storage of data retrieved for research purposes from other public sources, such as the genomic resources established by the NIAID. The data management system shall be a commercially available or well-established open source, documented, and supported relational database management system. Develop, utilize and update software applications for populating and updating the database; provide query capabilities, web and graphical user interfaces to the database; and develop software applications to export data in a variety of formats and to submit experimental data, clones and reagents to public repositories.

3) IT and Network Systems

Provide and maintain a secure, internal IT systems and network architecture, software development environment and computational infrastructure to support the modeling activities, algorithms and software applications development, data analysis and integration, data dissemination and other computational needs of the Projects of the Systems Biology Program. The Contractor's institution's security policies and guidelines must be followed. Provide a System Security Plan of the program infrastructure to the Project Officer within 3 months of award.

D. Systems Biology Working Group

In conjunction with the Project Officer, the Contractor shall establish a Systems Biology Working Group (SBWG). One SBWG will be established for all the Systems Biology Programs. The SBWG will be composed of approximately ten (10) investigators that are independent from the Systems Biology Programs and not collaborators. Those scientists should be knowledgeable in multiple research areas including, for example, microbiology, infectious diseases, immunology, genomics, proteomics, metabolomics and other advanced technologies, computer science, modeling, bioinformatics and information technology. Members with expertise in more than one scientific area are preferred. The SBWG is expected to provide advice on the operations, scientific progress and data release guidelines of all the contracts awarded under this BAA and to make recommendations regarding future directions.

Within two (2) months from contract award, the Contractor shall recommend for approval by the Project Officer, ten (10) names of individuals for SBWG membership and provide information on their area of expertise and other relevant selection factors. Current collaborators of the Contractor are not eligible to be members of the SBWG. The Contractor shall NOT contact potential candidates regarding service on the SBWG until final approval by the Project Officer.

E. Biocontainment, Safety And Training

- 1) Where applicable, provide facilities and resources to conduct work in accordance with the Biosafety Level (BSL) 2 and 3 guidelines (<http://www.cdc.gov/od/ohs/biosfty/bmb15/bmb15toc.htm>)
- 2) Provide protective garments, equipment and monitoring to assure safe handling of potentially infectious and hazardous microorganisms for all personnel involved.
- 3) Where applicable, ensure the conduct of work in accordance with DHHS regulations regarding the transfer of Select Agents (U.S. Code of Federal Regulations 42 C.F.R. Part 73, 7 C.F.R. Part 331, and 9 C.F.R. Part 121 (<http://www.cdc.gov/od/sap/index.htm>)).
- 4) Where applicable, ensure the conduct of work in compliance with the Federal Guideline For Research Involving Recombinant DNA molecules (<http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html/>).
- 5) Provide training for all personnel involved in the operation of and in conducting work in BSL 2 and BSL 3 biocontainment facilities with respect to the safe handling of potentially infectious and hazardous microorganisms, and Select Agents, and in the safe handling of recombinant DNA molecules.

F. Project Management and Administration

1) Overall Project Management

Provide a technical and administrative management infrastructure to ensure the efficient planning, implementation, oversight, and completion of all research Projects carried out under this contract and effective communications with the Project Officer and Contracting Officer. This infrastructure shall include:

- a. A Principal Investigator (PI) with ultimate responsibility for the scientific and technical leadership of the Systems Biology Program and the management, coordination and integration of all contract activities, including directing the research, meeting milestones, managing subcontracts and equipment purchases and making a wide range of decisions about staffing, research priorities, utilization of new experimental technologies, intellectual property issues, preparing contract required reports, deliverables and other official documentation.
- b. A Project Manager (PM) with overall responsibility for project management of the Systems Biology Program, including assisting the PI in fostering of communication and coordination across multidisciplinary research teams of investigators or of subcontractors, preparing progress reports and other deliverable documentation, monitoring the budget, tracking Projects' performance and timelines, making recommendations for changes to the Systems Biology Program activities and their timelines, and providing overall support to the activities of the PI.

- c. Other key scientific and technical staff with the relevant expertise to accomplish the technical requirements of the negotiated Statement of Work.

2) Program Development Plan

Within one (1) month from contract award, the Contractor shall submit to the Contracting Officer and Project Officer for their review and approval, a Program Development Plan that delineates any changes to the original Technical Proposal resulting from Scientific Review Group (SRG) recommendations and final negotiations with the Contracting Officer. Updates to the Program Development Plan shall be submitted on an annual basis as part of the Annual Progress Reports. The Program Development Plan and its updates are subject to modifications by the Contracting Officer and Project Officer prior to their approval. Any changes to the planned activities, timelines, milestones and deliverables of the Systems Biology Program and its research Projects carried out by the Contractor shall be commensurate with the complexity of the technical requirements of the negotiated Statement of Work.

The Program Development Plan shall include:

- a. a description of key goals and objectives of the Systems Biology Program and its Projects;
- b. any changes to the originally proposed technical approaches to be used to carry out the Systems Biology Program and its research Projects, and any changes to the physical facilities, equipment, and other resources to be made available to the Program;
- c. an organizational chart of the Systems Biology Program and its research Projects, including all the scientific, technical and administrative personnel, subcontractors, consultants and collaborators, and a brief description of their qualifications, relevant experience, role and percent effort committed to the Program or research Projects;
- d. any changes to the methods for ensuring frequent interactions and communication within and among the research teams; and
- e. delineation of the milestones of the Systems Biology Program and of each research Project, and timelines for the initiation, conduct and completion of each milestone.

3) Intellectual Property

The Contractor shall be solely responsible for the timely acquisition of all appropriate proprietary rights, including intellectual property rights, and all materials needed to perform the project. Before, during, and subsequent to the award, the U.S. Government is not required to obtain for the Contractor any proprietary rights, including intellectual property rights, or any materials needed by the Contractor to perform the project. The Contractor is required to report to the U.S. Government all inventions made in the performance of the project, as specified at FAR 52.227-11 (Bayh-Dole Act).

4) Reports and Deliverables

The Contractor shall provide all reports and other deliverables listed in the "Reporting Requirements and Other Deliverables" section of this BAA as they relate to the Contractor's specific Statement of Work.

5) Contract Meetings and Teleconferences

- a) Post-Award Initiation Meeting: Within thirty (30) calendar days of the effective date of the contract, the Contractor shall plan, conduct and be responsible for the logistical arrangements for a post-award initiation meeting to be held at a site within the Bethesda, Maryland area. The PI, Project Manager, all key investigators, shall attend this meeting. The purpose of this meeting shall be to review the Program Development Plan and to coordinate activities and communication. The PI shall provide slide presentations and a detailed summary of meeting discussions to the Project Officer and the Contracting Officer within twenty-one (21) calendar days following the date of the meeting. SBWG members may attend if they have been named and approved prior to the initiation meeting.
- b) Monthly Meetings/Teleconferences: The Contractor shall plan and conduct monthly meetings of the PI and PM with the Project Officer and Contracting Officer, either in person or via teleconference, to apprise them of technical achievements or hurdles related to the Projects' goals and objectives, and to discuss any issues/problems that are relevant to the scientific and financial administration of the Program and its future activities. The schedule for those meetings will be established in conjunction with the Project Officer and the Contracting Officer after contract award. Prepare and submit the agenda and meeting/teleconference materials to the Project Officer and other participants for their review no less than two (2) calendar days in advance of the meeting/teleconference, and prepare and submit meeting summaries to the Project Officer and participants within seven (7) calendar days after each meeting/teleconference. Include all meeting and teleconference summaries in the Semi-Annual and Annual Progress Reports.
- c) Annual Programmatic Meetings: One Annual Programmatic Meeting shall be held for all Systems Biology Programs. Contractors shall alternate responsibilities for organizing and conducting the meeting. The Project Officer will inform the Contractor of the schedule of meeting responsibility after contract award. The purpose of the Annual Programmatic Meeting is to share methodologies and findings, and to foster collaborations among the Programs. The Contractor shall be responsible for all costs incurred for conducting the logistical tasks associated with the meeting. The location of the meeting shall be at a site proposed by the Contractor and approved by the Project Officer and Contracting Officer. Prepare and submit the agenda and meeting materials to the Project Officer and the Contracting Officer for review and approval no less than thirty (30) calendar days in advance of the meeting, distribute meeting materials to all meeting participants within fourteen (14) calendar day of the meeting, and prepare and submit the electronic copies of the presentations to the Project Officer within fourteen (14) calendar days after each meeting. The meeting shall be attended by the Project Officer, the Contracting Officer and other key

NIAID and NIH staff, and by a maximum of five individuals from each Systems Biology Program, including subcontractor personnel.

- d) Annual SBWG Meetings: One Annual SBWG Meeting shall be held for all Systems Biology Programs in conjunction with the Annual Programmatic Meeting. Contractors shall alternate responsibilities for organizing and conducting the meeting. The Project Officer shall inform the Contractor of the schedule of meeting responsibility after contract award. The Contractor shall be responsible for the travel expenses of the SBWG members and for all costs incurred for conducting the logistical tasks associated with the meeting. Prepare and submit the agenda and meeting materials to the Project Officer and the Contracting Officer for review and approval no less than thirty (30) calendar days in advance of the meeting, distribute meeting materials to all meeting participants within fourteen (14) calendar day of the meeting, and prepare and submit meeting summaries to the Project Officer, SBWG members and other meeting participants within fourteen (14) calendar days after each meeting. Include the summary of the SBWG meeting in the Annual Progress Report. The meeting shall be attended by the Project Officer, the Contracting Officer and other key NIAID and NIH staff, and by a maximum of five individuals from each Program, including subcontractor personnel.

6) Annual site visits

Arrange for site visits at the Contractor's site on an annual basis, as requested by the Project Officer or the Contracting Officer.

7) Ad hoc Reports

Prepare and provide up to three (3) *ad hoc* reports per year to the Project Officer and Contracting Officer, as requested, on topics that fall within the technical requirements of the negotiated Statement of Work. Only with the approval of the Project Officer may the information contained within the *ad hoc* reports be provided to various branches of the Government and/or public health related agencies and collaborators. The Project Officer will specify the report format at the time of the request.

G. Publications, Press Releases and Advertising Materials

All manuscripts, abstracts, and book chapters containing data generated under this contract, and all brochures, newsletters and printed materials describing the Systems Biology Program's accomplishments and activities shall be submitted electronically to the Project Officer and Contracting Officer for review thirty (30) calendar days before submission for public presentation, distribution, or for consideration for publication. All press releases shall be submitted electronically to the Project Officer and Contracting Officer for review five (5) calendar days prior to issuing a press release. The Project Officer will review all manuscripts, abstracts, book chapters, brochures, newsletters, and printed materials in a period of time not to exceed fifteen (15) calendar days, and will provide written recommended changes. If Project Officer comments are not provided within these timelines, the Contractor may proceed with public presentation, distribution, or publication.

H. Final Transition

Plan and implement an orderly, safe and efficient transition to a subsequent contractor or to the Government, by the expiration date of the contract, including a comprehensive inventory of all the accumulated data and resources, the transfer and movement of stored reagents, data, web portals, databases, software applications and algorithms, SOPs, technologies, purchased supplies and equipment, and any other resource generated under this contract.

- 1) Prepare and submit, for review and approval by the Project Officer and the Contracting Officer, a written draft Final Transition Plan twelve (12) months prior to the completion date of the contract. The draft Final Transition Plan shall detail how the resources generated under this contract shall be transferred in an orderly manner to a subsequent contractor or the Government.
- 2) The Final Transition Plan shall be submitted ten (10) months prior to the completion date of the contract. Implement the Final Transition Plan, as approved by the Project Officer and the Contracting Officer by the end of the contract period of performance.
- 3) The Contractor shall maintain full operational capability until the completion date of the contract.